AF/1651, 1654

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/464,414
Filing Date	12/16/1999
First Named Inventor	Yasmin Thanavala
Art Unit	1651
Examiner Name	M. Flood
Attorney Docket Number	RPP:156C US

Total Number of Pages in This Submission: 53

ENCLOSURES *(Check all that apply)*

- [x] Fee Transmittal Form
- [ ] Fee Attached
- [ ] Amendment/Reply
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- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
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- [ ] After Allowance communication to Technology Center (TC)
- [x] Appeal Communication to Board of Appeals and Interferences
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Dunn & Associates
Signature	Michael L. Dunn
Date	October 17, 2003

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FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☑ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($)

Complete if Known	
Application Number	09/464,414
Filing Date	12/16/1999
First Named Inventor	Yasmin Thanavala
Examiner Name	M. Flood
Art Unit	1651
Attorney Docket No.	RPP:156C US

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☐ Deposit Account:

Deposit Account Number: 04-1790

Deposit Account Name:

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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below		Fee Paid
Total Claims		-20** =		X	=
Independent Claims		- 3** =		X	=
Multiple Dependent					=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

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SUBTOTAL (3) ($)

SUBMITTED BY				(Complete *(if applicable)*)	
Name (Print/Type)	Michael L. Dunn	*Registration No. (Attorney/Agent)*	25,330	*Telephone*	716-433-1661
Signature	Michael L. Dunn			*Date*	Oct 17, 2003

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RPP:156C US

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Yasmin Thanavala	Art Unit:	1651
Serial No:	09/464,414	Confirmation No:	7502
Filed:	December 16, 1999		
Examiner:	Flood, Michele		
For:	ORAL IMMUNOLOGY USING PLANT PRODUCT CONTAINING A NON-ENTERIC PATHOGEN ANTIGEN		

I certify that this **Revised Appeal Brief** is being deposited on **October 17, 2003** with the U.S. Postal Service as first class mail addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231

Michael L. Dunn
Registration No. 25,330

REVISED APPEAL BRIEF
(37 CFR 1.192)

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This is in response to the Notice of Non-Compliance with 37 CFR 1.192(c).

Applicants respectfully appeal the decision of the Examiner finally rejecting Claims 1-3, 7, 9, 10, 12, and 13 set forth in her Office Action dated April 22, 2002. A Notice of Appeal was mailed by the Applicants to the patent and Trademark Office on August 22, 2002 and received by the Patent and Trademark Office on September 3, 2002 as evidenced by a return postcard. Any required extension of time fees were authorized by an accompanying transmittal letter.

Real Parties in Interest

The real party in interest is Health Research, Inc., Assignee of the above application by assignment recorded in the Patent and Trademark Office at Reel 010626 Frame 0927.

Related Appeals and Interferences

Related Patent Applications 09/420,695 and 09/464,416 are currently on appeal.

Status of Claims

The application originally contained 19 claims. Claims 4-6, 8, 11-12, and 14-19 have been cancelled. No claims have been added by amendment. Claims 1-3, 7, 9, 10, and 13 are pending on Appeal.

Status of Amendments

Claims 1, 2, 3, 7, 9 and 10 have been amended. No amendments have been offered which have not been entered.

Summary of the Invention

As described in Claim 1 the invention comprises a method for providing a secondary boosting immune response in a mammal to a specific antigen of a non-enteric pathogen (NEPA). The pathogen is a pathogen that invades through a breach in the skin and that does not itself enterically raise a primary protective immune response in mammals in the absence of prior acquired immunity to the pathogen. The method includes the steps of: rendering the mammal immunoreceptive to the NEPA by prior immunization against a non-enteric pathogen containing the NEPA by vaccination by injection and then orally administering the NEPA to the immunoreceptive mammal by feeding the mammal with transgenic potato containing the NEPA

expressed in the potato to enterically cause a secondary immune response to the oral administration specific to the NEPA stronger than would be caused by orally administering the NEPA in the absence of the prior immunization by injection.

Issues Presented for Review

1. Whether claims 1-3, 7, 9-10 and 13 are patentable under 35 USC 112 first paragraph;

2. Whether claims 1-3, 7, 9-10 and 13 are patentable under 35 U.S.C. 112 second paragraph; and

3. Whether claims 1-3, 7, 9-10 and 13 are patentable under 35 U.S.C. 103(a) over U.S. Patent 5,914,123 to Arntzen et al. or U.S. Patent 6,136,320 to Arntzen et al. in view of Stites et al., Basic and Clinical Immunology, 7th ed., 1991 and further in view of admitted prior art.

Grouping of Claims

The claims do not stand or fall together. The subclaims further restrict the independent claims to particular species thus providing further argument against 35 U.S.C. 112 rejections, e.g. specific NEPA's are listed in claim 3 that are not listed in claim 1. Furthermore, the embodiments in the subclaims are not described in the cited art. Similarly, specific method steps, e.g. as claimed in claim 8 with respect to dosage levels, are not present in other claims and are not disclosed or suggested in the cited art.

Argument

Claims 1-3, 7, 9-10 and 13 have been rejected under 35 U.S.C. 112 first paragraph for lack of enablement. This rejection should be reversed. The rejection is based upon the allegation that enablement is not provided for providing an oral secondary immune response to

non-enteric pathogen antigens (NEPA's). This position by the Examiner is refuted, especially as it applies to the NEPA's selected from the group consisting of hepatitis C, hepatitis delta, yellow fever, dengue hemoragic fever, tetanus, staphylococcus aureous, yaws, relapsing fever, rat bite fever, bubonic plague and spotted fever as set forth in claim 3.

The rejection should be withdrawn since as previously discussed there is in fact clear enabling support in the specification, especially when considered in conjunction with the knowledge of one skilled in the art.

In making this rejection, the Examiner has said the specification "does not reasonably provide enablement for providing a secondary boosting response in a mammal to any and all NEPA's comprising the instantly claimed process steps and instantly claimed ingredients." and "the specification does not provide sufficient guidance as to how one of ordinary skill in the art would provide an immune response in a mammal and/or a human to a NEPA other than the non-enteric pathogen antigen, hepatitis B surface antigen" (emphasis added).

The Examiner's statement is insufficient to support the rejection. Enablement is not solely dependent upon the precise words of the specification, but must also include the knowledge of one skilled in the art. One skilled in the art clearly knows how to make the required genetically altered plant materials and in the 35 U.S.C. 103 rejections discussed infra, the Examiner has relied upon cited patents that clearly teach how to make the required plant materials and patents cited by the Examiner in fact have generically claimed such plant materials. This issue of enablement has thus already been decided by the U.S.P.T.O.

The Examiner's attention is drawn to U.S. Patent 5,679,880 in which claim 1 says:

"A transgenic plant, comprising and expressing a DNA sequence coding for an antigen of a pathogenic microorganism or an antigenic determinant thereof, said antigen or antigenic determinant thereof eliciting a secretory immune response in a human or other animal upon oral administration of tissue of said plant."

Similar disclosures and claims deemed supported by the U.S.P.T.O. are given in U.S. Patents 5,686,079 and 5,654,184.

Further, in the 35 U.S.C. 103 rejection, the Examiner has relied upon U.S. Patent 6,136,320 to Arntzen et al. Claim 1 of that patent says:

"An orally acceptable immunogenic composition comprising unpurified or partially purified recombinant viral immunogen expressed in a plant, wherein said immunogen is expressed in the plant at a level such that upon oral administration of said composition to an animal, an immunogenic response is observed."

Allowance of the above claims (and others) clearly shows that the patent office has accepted the fact that one skilled in the art now knows how to cause a plant to express a viral immunogen (antigen). If the Examiner were to maintain that one skilled in the art were not enabled to cause a plant to express an immunogenic viral antigen, she would, in essence, be taking a position that the patent she is relying upon contains an unsupported teaching and improperly supported claims. From a breadth perspective, the present application claims the same thing as U.S. Patent 6,136,320, except that in the presently claimed invention, it has been unexpectedly discovered that immunogens from non-enteric pathogens can be included that do not raise an oral primary immune response but can be used to obtain a secondary oral

immunogenic response, if the animal is first vaccinated (non-orally). The teachings in the specification are more than adequate to support this additional step for any viral immunogen within the previously accepted disclosure and claims of U.S. Patent 6,136,320.

Again it is clear that the U.S.P.T.O. has already decided that there is enablement for the base issues raised by the Examiner, i.e. one skilled in the art knows how to make plants and plant material expressing antigens from pathogenic microorganisms and further knows that they can be orally administered to obtain an immune response when the antigen is capable of eliciting such a response. The improvement in accordance with the present invention is that it has now been discovered that NEPA's which are otherwise not capable of eliciting any meaningful primary immune response orally, can be made to orally elicit a secondary immune response when the animal in question is previously vaccinated or immunized against the NEPA non-orally. This improvement is not obvious from the cited art but is clearly enabled by the teachings of the present specification in conjunction with the known state of the art.

The Examiner has further said "The art of virology, microbiology, and immunology are highly unpredictable because there are too many unknowns in the claimed process for the skilled artisan to be enabled to practice the invention commensurate in scope to the claimed invention." With due respect to the Examiner, in this particular case, she is in error. Since the publication of the present invention after filing, persons skilled in the art have repeatedly practiced the invention with respect to other non-enteric pathogen antigens. The Examiner's attention is, for, example called to the article by Webster et al., "Successful Boosting of a DNA Measles Immunization with an Oral Plant-Derived Measles Virus Vaccine", Journal of Virology, August

2002, pp. 7910-7912, where preparation of transgenic plants in the family *Solanaceae* was illustrated and such transgenic plants were used to orally induce a boosting response against measles. The Examiner's attention is further called to Warzecha et al, "Oral Immunology of Human Papillomavirus Virus-like Particles Expressed in Potato", the published abstract of the Fifth Annual Conference on Vaccine Research, May 6-8, 2002 held in Baltimore, Maryland wherein the actual preparation of potatoes containing sequences from papilloma virus and their use for orally boosting immune reaction using sub-immunogenic doses. **The proof is in the reality. One skilled in the art is clearly enabled to practice the invention as claimed because persons skilled in the art are in fact doing so and by the fact that the Examiner's position is contrary to the position already taken by the U.S. Patent and Trademark Office on numerous occasions.**

The Examiner should again be reminded that a patent specification is not intended to be a textbook including all information known and readily available to a skilled person. If such were not the case, every patent specification would be thousands of pages long rehashing known material ad nauseum and hiding the nature of the improvement of the invention within unnecessarily included information.

The Examiner is making the invention much more complicated than it is. The invention is easy to understand and can be practiced to the extent of the breadth of the claims by one of even meager skill in the art in view of the teachings of the specification.

Claims 1-3, 7, 9-10, and 12-13 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite.

This rejection should also be withdrawn.

The Examiner in arguing for ambiguity of the term "NEPA" is taking the definition of the term in the claims out of context leaving out the word "antigen" that is present in association with all definitions of "NEPA". Claim 1 clearly says "...a specific antigen of a non-enteric pathogen (NEPA)...". Page 5, line 5 of the specification referred to and misquoted by the Examiner actually says "Non-enteric pathogen **antigen**" (NEPA) means an **antigen** that will parentally raise an immune response to a non-enteric pathogen." (emphasis added). It is clear in the context of the claims and specification that "NEPA" refers to the antigen not to the entire pathogen. There is simply no ambiguity. Similarly, there is no ambiguity with respect to the fact that the active ingredient, i.e. NEPA, is in the vaccinating injection. Enumerating non-active ingredients is neither helpful nor required. Any person skilled in the art knows what vaccination by injection means. Further, it does not matter whether the vaccination is by a whole virus containing an NEPA or an isolated NEPA, so long as the NEPA is present and an immune response to the NEPA results. One skilled in art clearly knows this also.

The generic objection with respect to grammatical and idiomatic errors cannot be addressed. The generic objection is not understood. The objection is therefore improper and should be reversed.

The Examiner's objection to the lack of the word "boosting" in line 1 of amended claim 1 is formal in nature. The Examiner is correct that the omission of the word "boosting" is a typographical type error since the word "boosting" was never removed from claim 1 by the prior

amendment. The word "boosting" is therefore still clearly present in line 1 of claim 1. This objection was corrected in a response to the last official action.

It should, however be pointed out that the presence or absence of the word "boosting" in line 1 of claim 1 is irrelevant insofar as the meaning and breadth of the claim is concerned. The claim clearly requires providing a primary response followed by providing a secondary response. The provision of a secondary response as provided in claim 1 is known as a "boosting" response to one skilled in the art, whether or not the word "boosting" is actually present.

The Examiner has objected to claim 1 on the ground that "rendering the mammal immunoreceptive to the NEPA by injection" is indefinite on the ground that all mammals are immunoreceptive unless they have a compromised immune system. Again, the Examiner is taking terminology out of context. The exact quote should be "...rendering the mammal immunoreceptive to the NEPA by prior immunization against a non-enteric pathogen containing the NEPA by vaccination by injection..."

All normal mammals have limited immune response. As an example, normal mammals do not raise an immune response against "self" cells and do not rise an immune response against commonly encountered materials, e.g. water, vitamins, most carbohydrates, amino acids, etc. Normal mammals further do not raise an immune response to stimuli below a certain threshold concentration and may not raise a response to one method of exposure to an antigen while raising an immune response to another method of exposure to the same antigen. As an example some antigens may cause a serum response without causing a mucosal response and vice-versa.

The present claims make it clear that the immune response in question is specifically to an NEPA and not to any and all materials to which the mammal may or may not be immunoreceptive. The claims and specification further make it clear that the NEPA in question does not itself raise a protective enteric immune response in the absence of prior acquired immunity to render the mammal orally immunoreceptive to the NEPA. Normal mammals are not orally immunoreceptive to NEPA's unless they are first made orally immunoreceptive by prior immunization as claimed or by some other means. There is no ambiguity.

In view of the foregoing amendments and remarks, all objections and rejections under 35 U.S.C. 112 should be withdrawn.

Claims 1-3, 7, 9-10 and 13 have been rejected under 35 U.S.C. 103 as being unpatentable over Arntzen et al. (A, U.S. Patent 5,914,123) or Arntzen et al. (B, U.S. Patent 6,136,320 in view of Stites (U) and further in view of readily admitted prior art.

The rejection is improper and should be withdrawn for reasons previously discussed.

It is admitted that cited art discloses administration of immunogens expressed in plants to obtain an immune response; however, there is no suggestion of first administering the immunogen by injection and secondly administering the immunogen orally to obtain an oral response not otherwise obtained. None of the cited art in any combination suggests such a method. Such a concept is not obvious in view of the cited art. **Prior to the present invention, initial injection of an NEPA (alone or in a more complex viral package) followed by oral administration of the NEPA to obtain an immune response was never suggested and never tried.** Until the present invention, no person skilled in the art would have recognized

that an oral response to an NEPA, that does not normally yield an oral response, could be obtained by first obtaining a non-oral response, e.g. by injection.

The rejection is therefore clearly improper and should be withdrawn.

Arntzen et al. teaches a method for making a transgenic tobacco, tomato or potato that expresses HBsAg.

Notwithstanding the Examiner's assertion, **Arntzen et al. references do not teach "methods of making a transgenic plant expressing an immunogen derived from hepatitis B surface antigen, wherein the immunogen is capable of eliciting an immune response in an animal by consumption of the plant material."**

Arntzen et al. "A" itself teaches and recognizes that not all antigens would cause an immune response if ingested **and there is no suggestion as to how to make NEPA's raise an oral immune response. Until the present invention, it was simply not obvious.**

Arntzen et al. "A" says in column 15 beginning at line 27,

"The vaccines are conventionally administered parentally, by injection, for example either subcutanously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, ***in some cases***, oral formulations or aerosols." (emphasis added).

There is no teaching or suggestion in either Arntzen et al. reference of how the "some cases" could be determined; how the "some cases" could be accomplished or even more importantly how cases not within the ambiguous Arntzen "some cases" could be made to give an oral response when they normally would not.

While Arntzen et al. "A" suggests that tomato juice containing HBsAg **might** be used as a vaccine, in fact Arntzen provides no supporting data showing any immune response

whatsoever to tomato juice or any other plant containing HBsAg. To the extent that the Arntzen et al. references teach that tomato juice or any other plant material containing HBsAg can be used as a vaccine, they are inoperative references, since there is no teaching or suggestion as to how that might be done. ***Simply ingesting the plant material, as suggested by Arntzen et al., does not confer immunity.***

There is good reason for Arntzen's omission of data showing immune response to HBsAg by ingesting food material containing it, since prior to the present invention, in fact, there was little if any immune response whatsoever to HBsAg in orally ingested tomato juice or any other plant expressing HBsAg. **See the Rule 132 Declaration of Dr. Thanavala of record**. The response, if any, is clearly insufficient for that purpose.

Reference to the examples in the present specification clearly illustrates that priming of the subject of the immunization is required by either pre-vaccination or the use of an effective adjuvant. The Arntzen et al. references suggests neither. **The Arntzen et al. references simply do not suggest preimmunization by injection followed by oral feeding of a transgenic potato expressing a NEPA to obtain a secondary immune response as required by the present claims.**

Arntzen's suggestion of simple ingestion of plant material expressing HBsAg does not give a sufficient immune response to be considered protective. Arntzen discloses or suggests no way in which a high immune response could be orally obtained and the other cited references do not remedy that critical defect as previously discussed.

Simply making an unsupported suggestion in a reference without a teaching as to how the suggestion might be accomplished, is not a sufficient teaching to make a method for accomplishing the desired result obvious to one skilled in the art. Prophetic statements cannot be used to form the basis of a rejection, especially when they are unsupported and not true. In using the word "may" Arntzen is not saying that a response will occur, but only that it "might". In fact, simple ingestion of tomato juice containing an NEPA does not raise a protective immune response as shown by the Thanavala declaration.

The Arntzen et al. B reference 6,136,320 pays lip service to raising an immune response by ingestion, but in fact give no examples or teachings for obtaining such a result. **The only actual plant examples in Arntzen et al. relate to tomatoes and tobacco. There is no example of ingestion of either one to raise a primary or secondary protective immune response.** In fact, ingestion of the transgenic tomato does not raise any significant immune response (see the Rule 132 Declaration of Dr. Yasmin Thanavala of record) and certainly whole tobacco cannot be used for such a purpose because it is toxic and there is no reason to expect that it would work orally even if it could be ingested. **There is simply no teaching in either of the Arntzen et al. references of how oral immunization to any NEPA could be accomplished using a transgenic plant, and in fact the plants made in the Arntzen examples do not function orally to raise a primary protective immune response to any NEPA.** Arntzen certainly does not suggest that a potato expressing a NEPA could raise a secondary immune response when fed subsequent to immunization by injection, as presently claimed. **It is therefore clear that there is insufficient teaching or suggestion in the Arntzen**

et al. references to support a rejection of the present claims whether or not the references are considered alone or in combination with Stites.

Stites et al. adds nothing to cure the inadequate teachings and suggestions of the Arntzen et al. references. Stites et al. does not suggest anything concerning orally raising an immune response to an antigen expressed by a plant. Further, Stites et al. clearly does not suggest any method for **orally** raising a highly effective secondary immune response by feeding a potato expressing an antigen after prior injection of the antigen.

It is not clear how the Examiner is applying the "readily admitted prior art". The admission cited by the Examiner says that "Plants expressing hepatitis B surface antigen (HBsAg) have in fact been developed but have disappointingly been found to create little or unacceptably low immune responses in animals ingesting them..." The Appellants agree that there is an admission that plants have been developed expressing hepatitis B surface antigen. **This admission has been accepted by the Examiner for purposes of 35 U.S.C. 103 but apparently denied by the Examiner for purposes of 35 U.S.C 112.** There is certainly no admission that it was known that oral immunity could be obtained to an NEPA that does not normally raise oral immunity. An admission that one skilled in the art can make a plant that expresses an NEPA is hardly an admission of any suggestion that an oral immune response could be obtained to the NEPA that does not normally raise such a response. The only admission made, i.e. that one skilled in the art knows how to make a plant that expresses an NEPA, does not suggest how to obtain an oral response to the NEPA. Since the other cited art

similarly does not suggest how to obtain an oral immune response to an NEPA, the combination can hardly suggest the presently claimed invention.

All rejections should be reversed, which action is courteously requested.

Respectfully submitted,

Dated: October 17, 2003

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MLD/cah

Appendix

Reprinted below are the claims on appeal:

1. A method for providing a secondary boosting immune response in a mammal to a specific antigen of a non-enteric pathogen (NEPA), the pathogen being a pathogen that invades through a breach in the skin and that does not itself enterically raise a primary protective immune response in mammals in the absence of prior acquired immunity to the pathogen, said method comprising: rendering the mammal immunoreceptive to the NEPA by prior immunization against a non-enteric pathogen containing the NEPA by vaccination by injection; and then orally administering the NEPA to the immunoreceptive mammal by feeding the mammal with transgenic potato containing the NEPA expressed in the potato to enterically cause a secondary immune response to the oral administration specific to the NEPA stronger than would be caused by orally administering the NEPA in the absence of the prior immunization by injection.

2. The method of Claim 1 where the mammal is a human.

3. The method of Claim 2 wherein the NEPA is an antigen specific to a non-enteric pathogen selected from the group consisting of those that cause hepatitis B, hepatitis C, hepatitis delta, yellow fever, dengue hemorrhagic fever, tetanus, yaws, relapsing fever, rat bite fever, bubonic plague and spotted fever.

7. The method of Claim 2 wherein the human ingests sufficient plant material to provide from about 10 to about 100 micrograms of NEPA per kilogram of body weight of the human.

9. The method of Claim 7 wherein the human ingests sufficient plant material to provide from about 2 to about 5 grams of plant material per kilogram of body weight of the human.

10. The method of Claim 9 wherein the human ingests said plant material a plurality of different times, said times being separated from each other by at least 5 days.

13. The method of Claim 10 wherein the plurality of times is three times.